

Serial No.: 09/489,101

- 6 -

Art Unit 1632

REMARKS

Claims 1, 2, 7, 16, 50, 52, 63, 65, 70-72, 78-80, 85, 88, 98, 102, 109, 115, 118, 121, 125, 126 and 128-135 were previously pending in this application. By this amendment, Applicant is canceling claims 7, 16, 50, 52, 63, 65, 70-72, 78-80, 85, 88, 98, 102, 109, 115, 118, 129 and 133 without prejudice or disclaimer. Claims 1, 128 and 132 have been amended. As a result claims 1, 2, 118, 121, 125, 126 and 128-135 are pending for examination, with 1, 128 and 132 being independent claims. No new matter has been added.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1, 2, 118, 121, 123, 125, 126 and 128-135 as not enabled by the specification. Applicant has amended claim 1, 128 and 132 and respectfully requests reconsideration.

Applicant has amended the claims to recite specifically the type of cancer that the method can diagnose. For example, for the SOX genes, the cancer is small cell lung cancer. For the ZIC2 gene, a number of cancers are listed based on the expression results provided in a working example in Applicant's specification. These cancers have been expressly recited in claim 132. The dependent claims that previously recited the specific cancers have been canceled.

Applicants also have maintained the prior exclusion of normal tissues in which the genes are expressed. For example, for the SOX2 gene, claim 128 excludes brain, testis, prostate, small intestine and colon tissues from the samples that can be examined for the presence of small cell lung carcinoma, because these tissues were shown to express SOX2 (see the working examples in the specification). The samples should not require further limitation, e.g., to lung tissue for small cell lung cancer, because it is well known in the art that cancer cells of one type can metastasize and migrate to other tissues in the body. For example, the following small cell lung cancer cell lines are available from ATCC; each of these cell lines were isolated from tissues other than a primary lung cancer:

Cell Line	Cancer	Tissue Source
NCI-H1184 carcinoma	small cell lung cancer	lymph node (lung) metastasis
NCI-H209 carcinoma	small cell lung cancer	bone marrow metastasis
NCI-H2107 carcinoma	small cell lung cancer	bone marrow metastasis
NCI-H128 carcinoma	small cell lung cancer	pleural effusion

Serial No.: 09/489,101

- 7 -

Art Unit 1632

Therefore, tissue sources other than lung can be positive for small cell lung cancer, and given that Applicant teaches the methods needed to examine these tissues, Applicant maintains that the claims as now amended are fully enabled by the disclosure of the specification.

The Examiner set forth several additional aspects to the enablement rejection, which are taken in turn here.

The Examiner stated that "The specification provides no specific guidance or teachings with regard to the level of interaction between the agent and the claimed nucleic acid molecule in order for detection of cancer." Office Action, page 6.

Applicant's response is that enablement is a measure of the adequacy of description in the specification for teaching one of ordinary skill in the art how to make and/or use the claimed invention. The enablement requirement exists so that the skilled person need not conduct undue experimentation in order to practice the claimed invention. The enablement requirement, however, takes into account the level of skill in the art, the amount of guidance in the specification, and various other factors that permit an analysis of whether undue experimentation would be required. Based on Applicant's teaching of specific sequences, and the limitation of the claims to detection of specific cancers using those specific sequences, the person of skill in the art would not be required to use undue experimentation. All that is needed is for the skilled person to screen a cell for the presence of the claimed sequences, or expression products thereof. This is a typical and routine clinical laboratory procedure. Applicant's experimental data regarding expression of the claimed sequences in cancer cell lines supports this view.

The Examiner, in contrast, has not provided any reasons why the person of skill in the art would be required to use undue experimentation. For example, the Examiner alleges that "there is no indication of a threshold which would be indicative of any cancer." This is not relevant given that the claimed invention relates to detection of specific cancers in cell types in which it experimentally demonstrated that there was no detectable expression of these sequences. Therefore, the concept of a threshold is meaningless; any detectable expression would be sufficient to be diagnostic of cancer, as would be recognized by the person of skill in the art.

Regarding the Examiner's assertion that the "mere presence of a particular transcript does not speak as to whether any protein is produced," (Office Action at page 6) Applicant respectfully urges the Examiner to take note of the fact that each of the sequences used in the claimed methods are known genes that are known to make protein. In addition, the genes must

Serial No.: 09/489,101

- 8 -

Art Unit 1632

have been expressed (both transcribed and translated) in the cancer cells as is evidenced by the specific antibody response in the patients. These antibodies were used in the SEREX cloning procedure to isolate the genes, as is described in the specification (see Example 1: "Isolation of Immunoreactive clones from SCLC cell lines by SEREX"). Therefore, protein must have been produced from these genes.

The Examiner's statement that the specification does not identify any open reading frame or polypeptides for the sequences is not sufficient to support this enablement rejection. It must be remembered that the specification is directed to the person of skill in the art; Applicant's identification of the genes to be used in these methods is certainly enough to identify the genes, the open reading frames and the encoded polypeptides to one of ordinary skill in the art. Again, these genes are all known in the art.

The Examiner has not basis whatsoever to remark that one of ordinary skill in the art would have "reasonable doubt that the particular sequences claimed would be useful as a cancer marker sequence" (Office Action, page 6) in view of the working examples and Applicant's description of the use of the claimed sequences in methods of detection. On the contrary, Applicant's guidance and working examples would provide one of ordinary skill in the art with a reasonable expectation that the claimed methods would work as indicated.

The Examiner also stated that "it is unlikely that the simple presence of a sequence, as those claimed, would be diagnostic for any type of cancer." Office Action, page 6. First, Applicant claims detection of specific types of cancer, not any type. More importantly, Applicant has taught one of ordinary skill in the art which cancer cells and tissues express specific well-known genes, each of which was not known previously to have a cancer-associated expression pattern. The Examiner's assertion that there are many published marker sequences does not provide any specific reason for doubting the enablement of the claimed invention, given Applicant's description and working examples.

The Examiner's assertion that it would not be possible to diagnose any type of cancer on page 7 of the Office Action is obviated by the claim amendments.

Finally, in view of the amendments to the claims to restrict the method to specific cancers, no further experimentation would be required for one of ordinary skill in the art to use the methods claimed and described by Applicant as diagnostic methods for cancer. The

Serial No.: 09/489,101

- 9 -

Art Unit 1632

methodology is well known in the art, and the skilled person could readily use the claimed methods based on Applicant's teachings.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1, 2, 118, 121, 123, 125, 126 and 128-135 as indefinite for use of the term "specifically". Applicant respectfully traverses the rejection.

The Examiner states that the term "specifically" is a relative term that renders the claim indefinite. Applicant believes that one of ordinary skill in the art would not have difficulty ascertaining the scope of the invention, because an agent as used in the claims either binds specifically or not. For example, an agent that binds ZIC2, as used in the claims, would have to bind to ZIC2 and not other molecules within the limits of detection of the claimed assay. The person of skill in this art is familiar (highly familiar, in fact) with nucleic acid molecules, proteins and other agents that specifically bind in order to be used in a diagnostic assay.

Examples of such agents used in standard clinical assays include PCR primers, antibodies, etc.

Based on the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Serial No.: 09/489,101

- 10 -

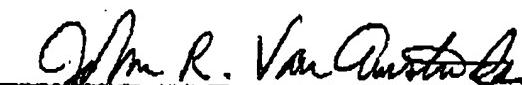
Art Unit 1632

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Gure, et al., Applicant


John R. Van Amsterdam, Reg No. 40,212
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210
Telephone: (617)720-3500

Docket No.: L00461.70073.US

Date: August 13, 2003
x08/15/03x

COP

Serial No.	09/489,101	File No.	110461-70073-US	By	JRV/jmw	
Title	Small Cell Lung Cancer Associated Antigens & Uses Therefor					
Application of Cure, et al.						
The U.S. PTO Mail Room acknowledges receipt of the following on the date stamped hereon:						
<input type="checkbox"/>	Mailing by Express Mail (37 CFR 1.10)	Provisional Application Cover Sheet				
Express Mail Label No. _____						
<input type="checkbox"/>	Patent Application	Multiple Dependent Claim Fee Sheet				
<input type="checkbox"/>	Non-provisional	<input type="checkbox"/> Provisional	Int'l. Clad. Standard, PRO Form 1449			
Inc. _____ pages, (_____) Abstract, (_____) Specification, (_____) Drawings, (_____) Declaration(s), (_____) Claims, (_____) # claims)						
<input type="checkbox"/> References Cited						
<input type="checkbox"/> Patent Document(s) # _____						
<input type="checkbox"/> Copy of Notice to File Unsigned Parts						
<input type="checkbox"/> Amendment/Response A/P						
<input type="checkbox"/> Petition for Ext. of Time (12)						
<input type="checkbox"/> Issue Fee Transmittal						
<input type="checkbox"/> Letter to Official Dispenser						
<input type="checkbox"/> Notice of Appeal						
<input type="checkbox"/> Brief (#3)						
<input type="checkbox"/> Check for \$ _____ Check # _____						
<input type="checkbox"/> Transmittal Letter (02)						
<input type="checkbox"/> Cont. of Mailing under 37 CFR 1.8(e)						
Assignment and Cover Sheet						
Verbal Statement claiming small entity status						
Fee calculation sheet (p2)						
CPA Transmittal						
<input type="checkbox"/> Other						

RECEIVED
U.S. PATENT AND TRADEMARK OFFICE
MAY 13 2003

DATE MAILED 8/13/03